



The 8th International Electronic Conference on Medicinal Chemistry (ECMC 2022)

01-30 NOVEMBER 2022 | ONLINE

Rapid and synchronized dormancy-breaking jumbo leek bulb inhibits postprandial carbohydrate degradation and absorption to be assumed preprandial ingestion

Chaired by **DR. ALFREDO BERZAL-HERRANZ**;
Co-Chaired by **PROF. DR. MARIA EMÍLIA SOUSA**



pharmaceuticals



Toshihiro Ona^{1,2,*}, and **Junko Johzuka**^{2,1}

¹ Graduate School of Bioresource and Bioenvironmental Sciences, Kyushu University, Kasuga, Fukuoka, Japan;

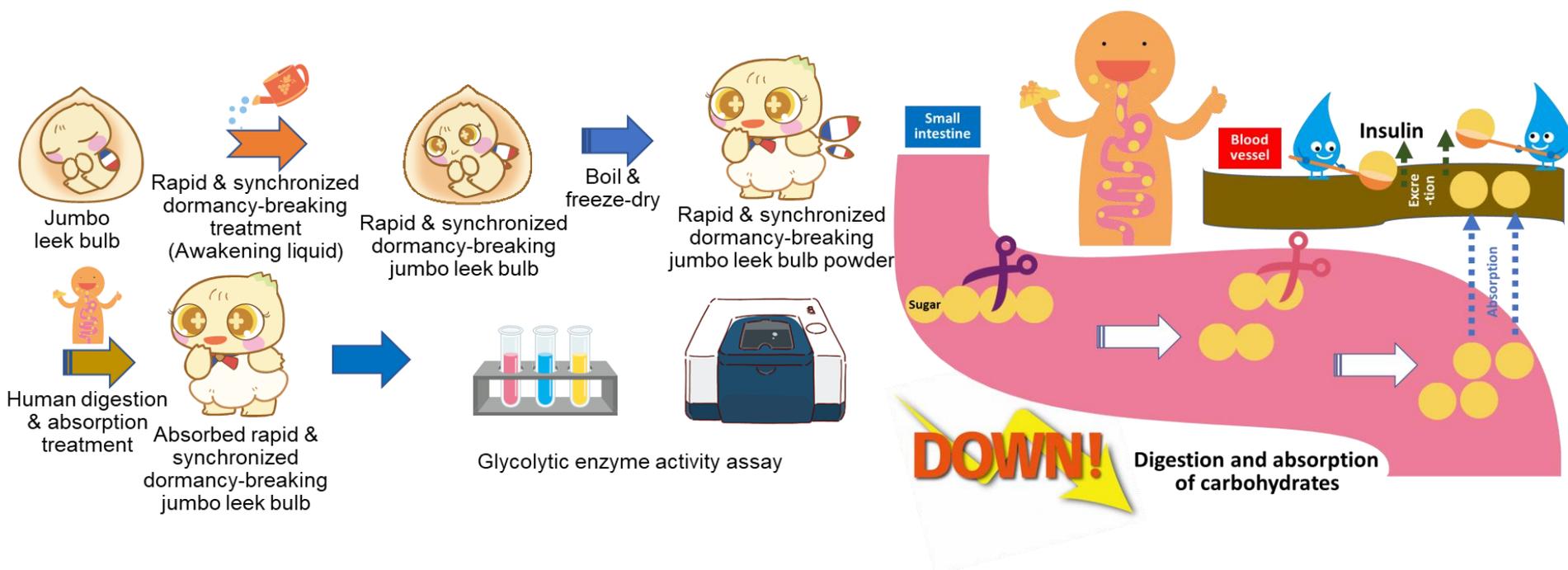
² O'Atari Inc., Onojo, Fukuoka, Japan;

* Corresponding author: ona@agr.kyushu-u.ac.jp, ona@oatari-inc.com



Rapid and synchronized dormancy-breaking jumbo leek bulb inhibits postprandial carbohydrate degradation and absorption to be assumed preprandial ingestion

Graphical Abstract



ECMC
2022

The 8th International Electronic
Conference on Medicinal Chemistry
01-30 NOVEMBER 2022 | ONLINE

Abstract: In order to prevent obesity and diabetes, it is important to avoid overeating, especially carbohydrates. Therefore, we evaluated the effect of taking jumbo leek bulb before a meal on the decomposition and absorption inhibition of carbohydrates after a meal. In this case, we used a product that was heat-treated after promoting phase transition of its content by rapid and synchronized dormancy-breaking (RSDB), and investigated by decreasing two enzyme activities, namely pancreatic α -amylase and α -glucosidase, and report the results. In pancreatic α -amylase, 6.5% inhibition of enzyme activity was observed in the untreated (heat and lyophilized) without RSDB compared to the control. In contrast, the RSDB inhibited it more effectively by 12.5%. In the case of α -glucosidase, 9.1% of inhibition of enzyme activity was observed in the untreated, whereas 14.6% was inhibited by the RSDB treatment, about 1.6 times more effective than the untreated. Thus, the RSDB jumbo leek bulb, when taken before a meal, was found to inhibit postprandial carbohydrate decomposition and absorption (postprandial hyperglycemia prevention effect). It is possible that the inulin in the jumbo leek has an inhibitory effect on glucose absorption by wrapping the carbohydrates, but the RSDB treatment may have accelerated the effect. Furthermore, an enhancement effect of insulin production and efficiency is expected by organosulfur compounds. In conclusion, the high efficacy of the RSDB jumbo leek in suppressing postprandial carbohydrate degradation and absorption was observed in a model experiment. The RSDB jumbo leek bulb is expected to be effective in preventing obesity and diabetes.

Keywords: carbohydrate; diabetes; dormancy-breaking; jumbo leek; obesity

ECMC
2022

The 8th International Electronic
Conference on Medicinal Chemistry
01-30 NOVEMBER 2022 | ONLINE

Introduction

Rapid and synchronized dormancy-breaking jumbo leek (Awakened French Garlic Bulb™) was prepared using a proprietary Grandir recipe™. After the bulb contents (ingredients) are converted by themselves, the bulb is boiled and freeze-dried. This process increases the inhibition of carbohydrate degradation and absorption after a meal of the jumbo leek bulb. This will effectively prevent obesity and diabetes. The research was carried out at the Global Innovation Center, Kyushu University, Kasuga, Fukuoka, Japan.

ECMC
2022

The 8th International Electronic
Conference on Medicinal Chemistry
01-30 NOVEMBER 2022 | ONLINE

Background

Blood glucose is the concentration of glucose in the blood. During digestion in the small intestine, polysaccharides in food are broken down into disaccharides by the enzyme pancreatic α -amylase, which is secreted by the pancreas, and these disaccharides are further broken down into glucose by the enzyme α -glucosidase to be absorbed into the blood vessels [1]. When an elevated blood glucose level is detected, the hormone insulin is secreted by the pancreas, which transports glucose from the blood to the cells [2]. In the liver and muscles, glucose is converted into glycogen, which is energy, and in adipose tissue, it is stored as fat. Diabetes is caused by insufficient or ineffective secretion of insulin [3, 4].

Since diabetes can cause blindness, dialysis, amputation of legs, and even cancer, we decided to develop the product solving this [3, 4].

Jumbo leek (French garlic) is a member of the leek genus [5-12]. It is a different species from garlic and is a different variant of the same species of leek. It is native to the Mediterranean region and has been used as a traditional medicine since 3,000 BC. Its medicinal effects are much higher than those of ordinary garlic, and it has been reported to prevent obesity, diabetes, and arteriosclerosis (inhibits the breakdown and absorption of sugar after meals and lowers cholesterol), improve liver function (inhibits the absorption of alcohol and strengthens the liver), antibacterial, anti-inflammatory, inhibit gene mutation, boost immunity, neutralize toxins, tonic, and anti-cancer. From these, it has been called the “magic herb”.

The need for assured efficacy with minimized toxicity as food

Jumbo leek (French garlic) bulbs are in a dormant state in which growth activity is temporarily suspended until conditions are favorable for germination, with minimal metabolism and energy consumption [13]. In early summer, the bulb goes to sleep, wakes up in the fall, germinates, and goes back to sleep [14]. After winter, they wake up again from sleep in spring, sprout, and the bulbs enlarge and grow. For this reason, the components of jumbo leek bulb are insoluble in water when they are asleep, so that they do not run off when it rains. When it awakens from sleep, it transforms itself into a water-soluble form and uses it for its own growth [13]. In this process, carbohydrates, proteins, and fats are broken down to make sugars, amino acids, fatty acids, minerals, growth hormones, repair hormones, and immune-supporting components to prevent disease in preparation for sprouting. Additionally, extractives and extracts are acceptable, but real food is favorable to take without extraction or concentration considered from long human eating habits.

However, it is difficult to decide the endpoint of bulb awakening by a conventional method. More importantly, the ingredients become uneven if bulbs did not awake at the same time. Therefore, a rapid method of awakening the jumbo leek bulb synchronously was developed as proprietary Grandir recipe™ with 2 days of dormancy-breaking.

Here, it is very important to assess rapid and synchronized dormancy-breaking jumbo leek bulb in order to assure bioavailability and efficacy with toxicity.

ECMC
2022

The 8th International Electronic
Conference on Medicinal Chemistry
01-30 NOVEMBER 2022 | ONLINE

Study objectives

The objective of the *in vitro* study was to determine the efficacy on inhibition of postprandial carbohydrate degradation and absorption to prevent obesity and diabetes, and hepatotoxicity of rapid and synchronized dormancy-breaking jumbo leek (French garlic) in case of oral administration as food.



Methods (Fig. 1)

Sample

The organic jumbo leek (French garlic; *Allium ampeloprasum*) bulb was grown in Shimabara, Nagasaki, Japan. Rapid and synchronized dormancy-breaking was performed by our proprietary Grandir recipe™ using Awakening liquid™ (based on concentrated malt extract, edible; O'Atari Inc., Japan). Treated and untreated samples were boiled, freeze-dried and pulverized by a grinder and sieved to pass 60 mesh.

Digestion treatment

For the use of oral administration, the French garlic bulb powder was digested in the stomach step using pepsin for enzyme assay, and further digested in the duodenum step using a human model system including enzymes and bile extract. Then the fraction of molecular weight of 10,000 or less was filtered as an intestinal absorption fraction for hepatotoxicity assay [15-17].

Methods (Fig. 1)

Enzyme assay

Starch azul was used as substrate and porcine pancreatic α -amylase as enzyme, and α -amylase inhibitory activity was determined from the measurement of change in absorbance [18]. Using *p*NPG as substrate and yeast α -glucosidase as enzyme, α -glucosidase inhibitory activity was determined from the absorbance measurement of the reaction mixture [19].

Hepatotoxicity assay

Human liver cell line Hep G2 was used for hepatotoxicity assay. Exponentially growing cells were two-dimensionally cultured with the digested untreated and treated samples for 24h. The live cells were counted using trypan blue.

Methods (Fig. 1)

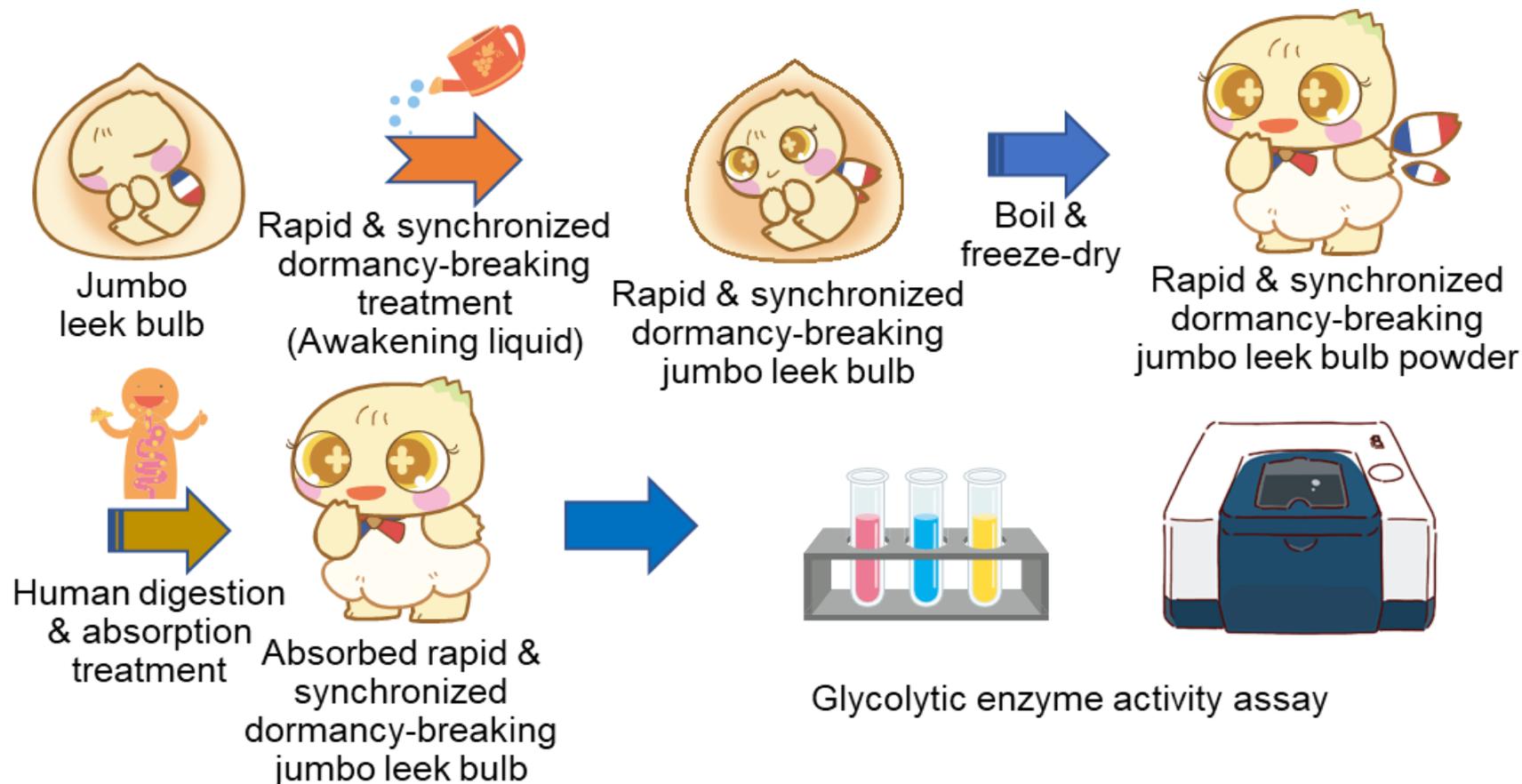


Fig. 1 Experimental scheme.

Results and discussion

Effects of inhibition of postprandial carbohydrate degradation and absorption

The postprandial carbohydrate degradation and absorption inhibitory effect of rapid and synchronized dormancy-breaking jumbo leek (French garlic) bulbs, intended for oral administration (eating), was tested by lowering the activity of two enzyme activities, namely pancreatic α -amylase and α -glucosidase [18, 19].

The results showed that, for pancreatic α -amylase, heating and freeze-drying samples that had not been subjected to rapid and synchronized dormancy-breaking (untreated) was effective in inhibiting enzyme activity by 6.5% compared to the control. In contrast, the rapid and synchronized dormancy-breaking sample showed an enhanced inhibitory effect of 12.5%, approximately double that of the untreated sample (Fig. 2). Next, the inhibitory effect of α -glucosidase was enhanced in the untreated sample (9.1%) and in the rapidly and synchronized dormancy-breaking sample (14.6%), which was about 1.6 times more effective than the untreated sample (Fig. 3). These results indicate that the rapid and synchronized dormancy-breaking jumbo leek bulbs have a significant inhibitory effect on the breakdown and absorption of postprandial carbohydrates (postprandial hyperglycemia-preventive effect).

Results and discussion

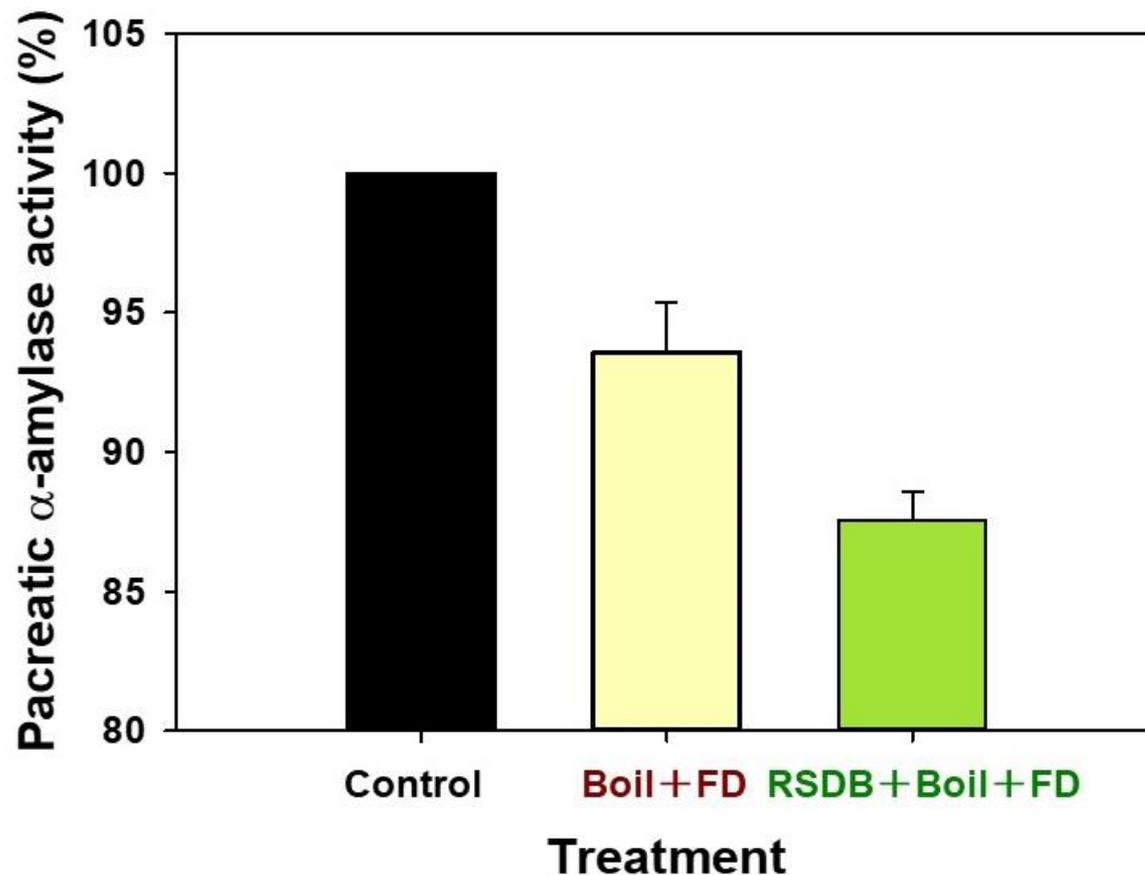


Fig. 2 Inhibition in enzymatic activity of α -amylase by rapid and synchronized dormancy-breaking (RSDB) jumbo leek bulb.

Results and discussion

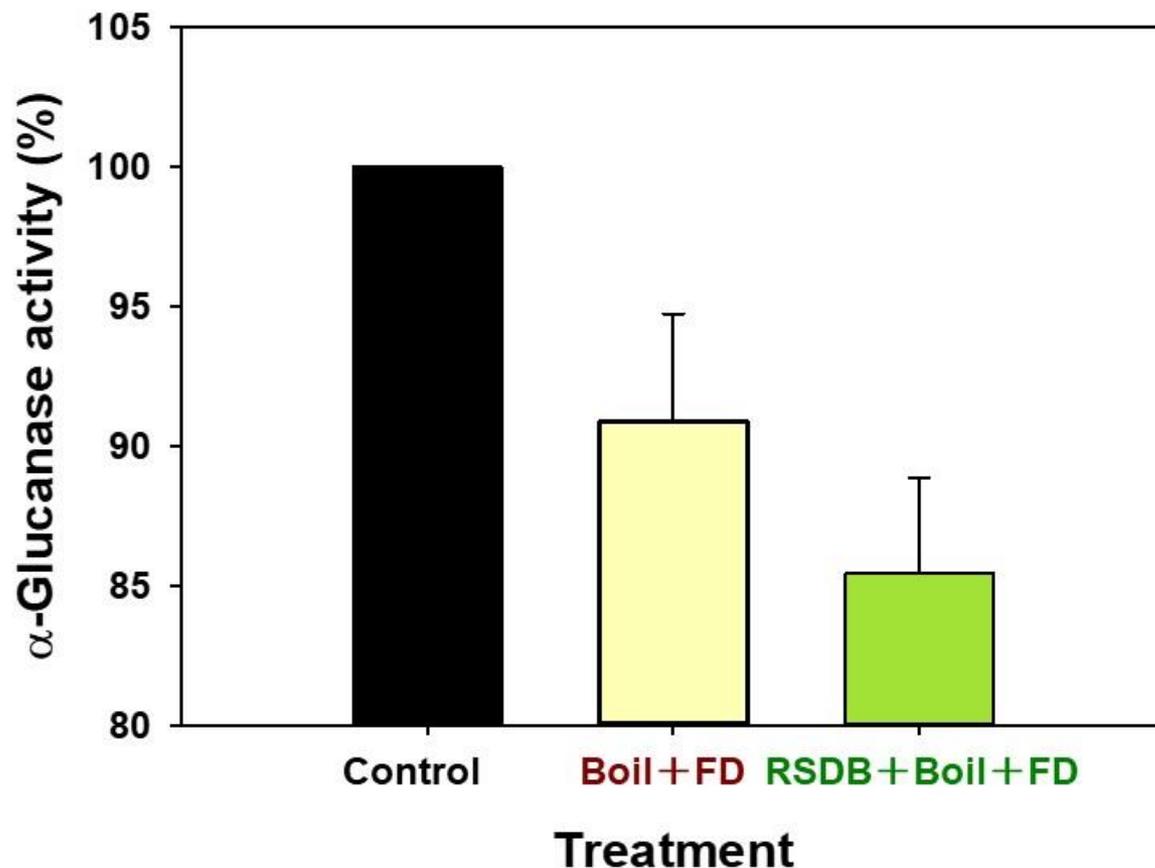


Fig. 3 Inhibition in enzymatic activity of α -glucanase by rapid and synchronized dormancy-breaking (RSDB) jumbo leek bulb.

Results and discussion

Effects on lowering hepatotoxicity

Rapid and synchronized dormancy-breaking jumbo leek (French garlic) bulb showed hepatotoxicity at a concentration of 3.75mg/ml, whereas untreated sample did so at a 1.25mg/ml. The hepatotoxicity of jumbo leek bulb was lowered 1/3 by rapid and synchronized dormancy-breaking treatment by Grandir recipe™ using Awakening liquid™.

Obese and diabetes prevention

Jumbo leek contains inulin as much as jerusalem artichoke [8, 20]. Therefore, inulin wraps around carbohydrates, increasing their absorption inhibition effect. Additionally, inulin has been reported to improve the secretion of insulin and appetite suppressant hormones, leading to weight loss and prevention of hyperglycemia [21, 22].

Results and discussion

Furthermore, jumbo leek contains organosulfur compounds such as alliin and S-allyl L-cysteine, which have been reported to promote both the production and effects of insulin, facilitating the elimination of sugar from the blood vessels [23-25]. Moreover, similar to garlic, in rapid and dormancy-breaking jumbo leek bulbs, the accumulation of isoalliin in preparation for germination, followed by green discoloration, probably due to the reaction between isoalliin and alliin [26-30]. Therefore, similar effects to other organosulfur compounds are expected from isoalliin [23-25, 29]. It is also high in saponins, which may be speculated to increase the effect of insulin [8, 30, 31].

In summary, it can be concluded that rapid and synchronized dormancy-breaking jumbo leek bulbs inhibit the action of enzymes that break down carbohydrates, hinder their breakdown and absorption, promote the production and effect of insulin, and stimulate the secretion of appetite suppressing hormones (Fig. 4). It is rare that such a wide range of effects can be obtained in a single food, and we have succeeded in making the “magic herb” highly functional in food form, without extracting or concentrating it. Eating the rapid and dormancy-breaking jumbo leek bulbs is expected to have a preventive effect on obesity through sugar dieting and appetite suppression, as well as a preventive effect on diabetes through its blood sugar lowering action with minimized toxicity.

Results and discussion

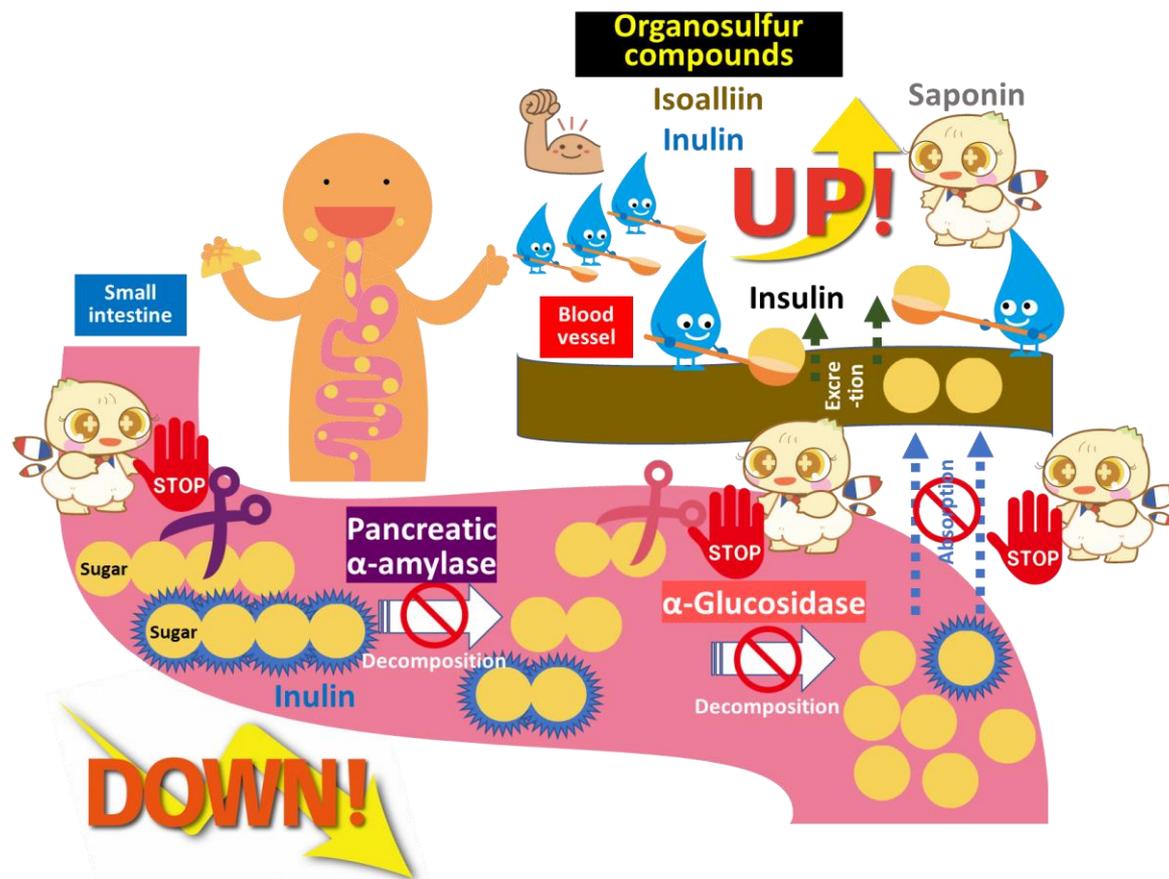


Fig. 4 Effect of rapid and synchronized dormancy-breaking (awakened) jumbo leek on inhibition of postprandial carbohydrate degradation and absorption, and blood glucose levels.

Conclusions

Rapid and synchronized dormancy-breaking jumbo leek (French garlic) bulb showed two things:

Suitable for fight against carbohydrate absorption after a meal with minimized toxicity by oral administration.

Suitable for therapy and prevention against obese and diabetes with minimized toxicity by oral administration.

Consequently, Awakened French Garlic Bulb™ is suitable for functional food supplement.

Acknowledgments

This research was supported by O'Atari Inc. and Kyushu University.



O'Atari Inc.



KYUSHU
UNIVERSITY

ECMC
2022

**The 8th International Electronic
Conference on Medicinal Chemistry**
01-30 NOVEMBER 2022 | ONLINE

References

- [1] Tundis, R., Loizzo, M. R., & Menichini, F. (2010). Natural products as α -amylase and α -glucosidase inhibitors and their hypoglycaemic potential in the treatment of diabetes: an update. *Mini Reviews in Medicinal Chemistry*, 10(4), 315-331.
- [2] DeFronzo, R. A., Ferrannini, E., Groop, L., Henry, R. R., Herman, W. H., Holst, J. J., Hu, F. B., Kahn, C. R., Raz, I., Shulman, G. I., Simonson, D. C., Testa, M. A., & Weiss, R. (2015). Type 2 diabetes mellitus. *Nature Reviews Disease Primers*, 1(1), 1-22.
- [3] Kim, J. S., Hyun, T. K., & Kim, M. J. (2011). The inhibitory effects of ethanol extracts from sorghum, foxtail millet and proso millet on α -glucosidase and α -amylase activities. *Food Chemistry*, 124(4), 1647-1651.
- [4] Bascones-Martinez, A., Gonzalez-Febles, J., & Sanz-Esporrin, J. (2014). Diabetes and periodontal disease. Review of the literature. *American Journal of Dentistry*, 27(2), 63-7.
- [5] Ariga, T., Kumagai, H., Yoshikawa, M., Kawakami, H., Seki, T., Sakurai, H., Hasegawa, I., Etoh, T., Sumiyoshi, H., Tsuneyoshi, T., Sumi, S., & Iwai, K. (2002). Garlic-like but odorless plant *Allium ampeloprasum* 'Mushuu-ninniku'. *Journal of the Japanese Society for Horticultural Science*, 71(3), 362-369.

References

- [6] Najda, A., Błaszczuk, L., Winiarczyk, K., Dyduch, J., & Tchórzewska, D. (2016). Comparative studies of nutritional and health-enhancing properties in the “garlic-like” plant *Allium ampeloprasum* var. *ampeloprasum* (GHG-L) and *A. sativum*. *Scientia Horticulturae*, 201, 247-255.
- [7] Devi, V., & Brar, J. K. (2018). Comparison of proximate composition and mineral concentration of *Allium ampeloprasum* (elephant garlic) and *Allium sativum* (garlic). *Chemical Science Reviews and Letters*, 7(25), 362-7.
- [8] Lim, T. K. (2013). *Allium ampeloprasum*. *Edible medicinal and non-medicinal plants: Volume 9, Modified Stems, Roots, Bulbs* (pp. 103-123). Springer Science & Business Media.
- [9] https://specialtyproduce.com/produce/Elephant_Garlic_850.php
- [10] Shelke, P. A., Rafiq, S. M., Bhavesh, C., Rafiq, S. I., Swapnil, P., & Mushtaq, R. (2020). Leek (*Allium ampeloprasum* L.). In *Antioxidants in vegetables and nuts – properties and health benefits* (pp. 309-331). Springer, Singapore.
- [11] Uchida, A., Kei, T., Ogihara, Jun, Matsufuji, H., Ohta, S., & Sakurai, H. (2008). Effects of jumbo leek on blood glucose level in streptozotocin-induced diabetic rats and liver damage in acetaminophen-treated rats. *Nippon Shokuhin Kagaku Kogaku Kaishi*, 55(11), 549-558.

References

- [12] Loppi, S., Fedeli, R., Canali, G., Guarnieri, M., Biagiotti, S., & Vannini, A. (2021). Comparison of the mineral and nutraceutical profiles of elephant garlic (*Allium ampeloprasum* L.) grown in organic and conventional fields of Valdichiana, a traditional cultivation area of Tuscany, Italy. *Biology*, 10(10), 1058.
- [13] Kigel, J. (Ed.). (1995). *Seed development and germination* (Vol. 41). CRC press.
- [14] McLaurin, W. J., Adams, D. B., & Eaker, T. (2009). *Garlic production for the gardener*. Cooperative extension, the University of Georgia college of agricultural and environmental sciences. Circular 854, 1-8.
- [15] Hollebeeck, S., Borlon, F., Schneider, Y. J., Larondelle, Y., & Rogez, H. (2013). Development of a standardised human in vitro digestion protocol based on macronutrient digestion using response surface methodology. *Food chemistry*, 138(2-3), 1936-1944.
- [16] Pastoriza, S., Delgado-Andrade, C., Haro, A., & Rufián-Henares, J. A. (2011). A physiologic approach to test the global antioxidant response of foods. The GAR method. *Food Chemistry*, 129(4), 1926-1932.
- [17] Rufián-Henares, J. A., & Morales, F. J. (2007). Effect of *in vitro* enzymatic digestion on antioxidant activity of coffee melanoidins and fractions. *Journal of Agricultural and Food Chemistry*, 55(24), 10016-10021.

References

- [18] Liu, J., Lu, J. F., Kan, J., Wen, X. Y., & Jin, C. H. (2014). Synthesis, characterization and *in vitro* anti-diabetic activity of catechin grafted inulin. *International Journal of Biological Macromolecules*, 64, 76-83.
- [19] Kim, J. S., Hyun, T. K., & Kim, M. J. (2011). The inhibitory effects of ethanol extracts from sorghum, foxtail millet and proso millet on α -glucosidase and α -amylase activities. *Food Chemistry*, 124(4), 1647-1651.
- [20] Munim, A., Rod, M. R., Tavakoli, H., & Hosseinian, F. (2017). An analysis of the composition, health benefits, and future market potential of the Jerusalem artichoke in Canada. *Journal of Food Research*, 6(5), 69-69.
- [21] Mudannayake, D. C., Wimalasiri, K. M. S., Silva, K. F. S. T., & Ajlouni, S. (2015). Selected Sri Lankan food plants and other herbs as potential sources of inulin-type fructans. *Journal of the National Science Foundation of Sri Lanka*, 43(1), 35-43.
- [22] Wan, X., Guo, H., Liang, Y., Zhou, C., Liu, Z., Li, K., Niu, F., Zhai, X., & Wang, L. (2020). The physiological functions and pharmaceutical applications of inulin: a review. *Carbohydrate Polymers*, 246, 116589.

References

- [23] Walag, A. M. P., Ahmed, O., Jeevanandam, J., Akram, M., Ephraim-Emmanuel, B. C., Egbuna, C., Semwal, P., Iqbal, M., Hassan, S., & Uba, J. O. (2020). Health Benefits of Organosulfur Compounds. In *Functional Foods and Nutraceuticals* (pp. 445-472). Springer, Cham.
- [24] Caroline, O. B., Ebuehi, O. A., Cecilia, O. A., & Kayode, O. A. (2021). Effect of *Allium sativum* extract in combination-with orlistat on insulin resistance and disrupted metabolic hormones in high fat diet induced obese rats. *Scientific African*, 14, e00994.
- [25] Augusti, K. T., & Sheela, C. G. (1996). Antiperoxide effect of S-allyl cysteine sulfoxide, an insulin secretagogue, in diabetic rats. *Experientia*, 52(2), 115-119.
- [26] Yamazaki, Y., Yamamoto, T., & Okuno, T. (2012). Causes and remedies for green discoloration of processed garlic puree: effects of storage conditions on ingredient bulbs. *Food Science and Technology Research*, 18(2), 187-193.
- [27] Kim, S., Kim, D. B., Jin, W., Park, J., Yoon, W., Lee, Y., Kim, S., Lee, S., Kim, S., Lee, O-H., Shin, Dongbin., & Yoo, M. (2018). Comparative studies of bioactive organosulphur compounds and antioxidant activities in garlic (*Allium sativum* L.), elephant garlic (*Allium ampeloprasum* L.) and onion (*Allium cepa* L.). *Natural Product Research*, 32(10), 1193-1197.

References

- [28] Melino, S., Leo, S., & Toska Papajani, V. (2019). Natural hydrogen sulfide donors from *Allium* sp. as a nutraceutical approach in type 2 diabetes prevention and therapy. *Nutrients*, 11(7), 1581.
- [29] Yamaguchi, Y., & Kumagai, H. (2020). Characteristics, biosynthesis, decomposition, metabolism and functions of the garlic odour precursor, S-allyl-L-cysteine sulfoxide. *Experimental and Therapeutic Medicine*, 19(2), 1528-1535.
- [30] Morita, T., Ushiroguchi, T., Hayashi, N., Matsuura, H., Itakura, Y., & Fuwa, T. (1988). Steroidal saponins from elephant garlic, bulbs of *Allium ampeloprasum* L. *Chemical and Pharmaceutical Bulletin*, 36(9), 3480-3486.
- [31] Elekofehinti, O. O., Ejelonu, O. C., Kamdem, J. P., Akinlosotu, O. B., & Adanlawo, I. G. (2017). Saponins as adipokines modulator: a possible therapeutic intervention for type 2 diabetes. *World Journal of Diabetes*, 8(7), 337.